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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,424	06/21/2001	Karl Kavalkovich	640100-426	4226

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EXAMINER
NAFF, DAVID M

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/831,424	Kawakovich et al
Examiner	**Group Art Unit**
Yoo	1657

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

X Responsive to communication(s) filed on 2/10/03.

X This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

X Claim(s) 1-29 is/are pending in the application.

Of the above claim(s) ____ is/are withdrawn from consideration.

Claim(s) ____ is/are allowed.

X Claim(s) 1-29 is/are rejected.

Claim(s) ____ is/are objected to.

Claim(s) ____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The proposed drawing correction, filed on ____ is approved disapproved.

The drawing(s) filed on ____ is/are objected to by the Examiner.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been received.

received in Application No. (Series Code/Serial Number) ____.

received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: ____.

Attachment(s)

Information Disclosure Statement(s), PTO-1449, Paper No(s).

Interview Summary, PTO-413

Notice of Reference(s) Cited, PTO-892

Notice of Informal Patent Application, PTO-152

Notice of Draftsperson's Patent Drawing Review, PTO-948

Other ____

Office Action Summary

The amendment of 2/10/03 canceled claims 1-11 and added claims 12-29.

Claims examined on the merits are 12-29 which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 16, 17, 21, 22, 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support is not readily apparent in the specification for the cell density ranges required by the claims. The page and lines should be pointed out where these ranges are recited. If not recited, how these ranges were derived should be described in detail.

Claim Rejections - 35 USC § 112

Claims 12-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Composition claims 12-17 are confusing by claim 12 reciting "cells are contacted with a chondroinductive agent" (bridging the last two lines). It is unclear as to when the cells are contacted with the agent, and whether the agent is to be part of the composition.

Method claims 18-22 are confusing by claim 18 reciting "cells are contacted with a chondroinductive agent" (last line). It is unclear when in the method, the cells are contacted with the agent.

Claim Rejections - 35 USC § 103

Claims 12-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grande et al (WO 96/28539) in view of Pittenger et al (WO 98/32333).

Claims 12-17 are drawn to a composition for producing cartilage containing human mesenchymal stem cells in an alginate gel, wherein the cells are contacted with a chondroinductive agent. Claims 18-22 are drawn to regenerating or repairing cartilage in an individual by administering human mesenchymal stem cells in an alginate gel, wherein the cells are contacted with a chondroinductive agent. Claims 21-29 are drawn to forming cartilage *in vitro* by admixing human mesenchymal stem cells with a solution of alginate, polymerizing the alginate to form an alginate gel layer containing the cells and contacting the cells in the gel layer with a chondroinductive agent.

Grande et al disclose (page 6, line 10 to page 7, line 9, and page 15) generating cartilage *in vivo* by forming an alginate solution containing human mesenchymal stem cells, injecting the solution where cartilage is to be generated, and gelling the alginate *in vivo*. Alternatively, the alginate may be gelled and the gelled alginate containing the cells implanted.

Pittenger et al disclose carrying out *in vitro* chondrogenesis with human mesenchymal stem cells in contact with a chondroinductive agent

such as TGF-β3 or a glucocorticoid (page 4, last paragraph), or a component of extracellular matrix such as hyaluronic acid (page 15, line 8 of first full paragraph and page 28, claims 30 and 31).

It would have been obvious to combine the human mesenchymal stem cells of Grande et al with a chondroinductive agent such as TGF-β3 or a component of extracellular matrix such as hyaluronic acid to obtain the chondroinductive function of the agent to induce differentiation of the human mesenchymal stem cells into chondrocytes as suggested by Pittenger et al. Pittenger et al would have further suggested carrying out chondrogenesis of mesenchymal stem cells *in vitro* when desiring to obtain chondrocytes for implanting.

Response to Arguments

Applicants urge that Grande et al does not use a chondroinductive agent. However, in view of Pittenger et al the use of this agent in combination with the human mesenchymal stem cells of Grande et al would have been obvious. The chondroinductive agent in the claims is being used for its expected function as taught by Pittenger et al. While Pittenger et al may use a pellet, this is not critical since the cells can be in a serum-free medium (page 4, second paragraph). There is insufficient evidence to establish that using an alginate gel provides improved differentiation as compared to differentiation obtained by Pittenger et al.

Claim Rejections - 35 USC § 103

Claims 12-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borland et al (WO 98/25653) in view of Grande et al and Pittenger et al.

The invention, Grande et al and Pittenger et al are described above.

Borland et al (WO 98/25653) disclose forming a partially hardened alginate gel (page 13, lines 15-29, and paragraph bridging pages 18 and 19) containing cells such as cells that form cartilage (page 26, lines 1-2) and injecting the partially hardened gel to form cartilage.

It would have been obvious to replace the partially hardened alginate gel of Borland et al with an alginate solution and inject the solution, or with a hardened alginate gel and implant the hardened gel as disclosed by Grande et al when injecting an alginate solution or implanting an alginate gel to form cartilage since using the alginate solution or gel would have been expected to provide the same type of result as when using partially hardened alginate gel. Using human mesenchymal stem cells as the cartilage forming cells of Borland et al would have been further suggested by Grande et al using human mesenchymal stem cells to form cartilage, and these cells would have been expected to provide the function of cartilage forming cells desired by Borland et al. When using an alginate solution or gel and human mesenchymal stem cells in Borland et al as set forth above, it would have been further obvious to combine the human mesenchymal stem cells with chondroinductive agent to obtain its function to induce differentiation of the human mesenchymal stem cells into chondrocytes as suggested by Pittenger et al. Pittenger et al would have further suggested carrying out chondrogenesis of

mesenchymal stem cells *in vitro* when desiring to obtain chondrocytes for implanting.

Response to Arguments

While Borland et al does not teach a chondroinductive agent, the use of such as agent would have been obvious from Pittenger et al for reasons set forth above when applying Pittenger et al. The comments in regard to Grande et al and Pittenger et al set forth above in response to arguments also apply to this rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is (703) 308-0520. The examiner can normally be reached on

Monday-Thursday and every other Friday from about 8:30 AM to about 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number (703) 308-4743.

The fax phone number is (703) 872-9306 before final rejection or (703) 872-9307 after final rejection.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DMN
5/19/03

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